

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re application of:

SNYDER *et al.*

Appl. No.: 09/849,781

Filed: May 4, 2001

For: **PROTEIN CHIPS FOR HIGH-
THROUGHPUT SCREENING OF
PROTEIN ACTIVITY**

Confirmation No.: 9891

Art Unit: 1639

Examiner: Wessendorf, Teresa D.

Atty. Docket: 2493.0010002/RWE/JKM

Declaration of Michael Snyder Under 37 C.F.R. § 1.132

Mail Stop Amendment

Commissioner for Patents

PO Box 1450

Alexandria, VA 22313-1450

Sir:

The undersigned, Michael Snyder, residing at 230 Somerset Avenue, Fairfield, CT 06824, USA, declares and states as follows:

1. I am a co-inventor of above-captioned U.S. Patent Application No. 09/849,781 ("the '781 application") entitled "Protein Chips for High-Throughput Screening of Protein Activity," which has a filing date of May 4, 2001, which claims benefit to U.S. Provisional Patent Application No. 60/201,921, filed May 4, 2000, and to U.S. Provisional Patent Application No. 60/221,034, filed July 27, 2000.

2. I am currently employed by Yale University, the assignee of the above-captioned application. I hold the positions of Director of the Yale Center for Genomics and Proteomics and Professor in the Departments of Molecular, Cellular and

Developmental Biology, and Molecular Biophysics and Biochemistry. My credentials are provided in the *curriculum vitae* that is attached to this declaration as Exhibit A. I received my Ph.D. degree in Biology from the California Institute of Technology in 1983, where my research was focused on *Drosophila* gene organization. As seen from my attached *curriculum vitae*, I have published many papers related to characterization of yeast and human proteomes, control of cell division and cellular morphology in yeast, and characterization of the human genome. I have received many honors and am involved in numerous professional and scientific societies related to genomics, proteomics and genetics. Based on my education and experience, I am an expert in the field of yeast and human genomics, proteomics, and molecular genetics.

3. I have reviewed and am familiar with the '781 application filed on May 4, 2001, the Office Action dated March 18, 2008 ("the Office Action"), issued by the U.S. Patent and Trademark Office in the present application, the references cited in the Office Action, and the currently pending claims, filed in the Reply to Office Action with this declaration.

4. In the Office Action, the Examiner asserts that the claims are allegedly not enabled. Specifically, the Examiner asserts that the specification does not enable the claimed array comprising 61 purified, active kinases and functional domains of kinases, from a mammal, yeast or *Drosophila*.

5. In making this declaration, it is my opinion that at the time this application was filed, a typical practitioner in the field of genomics and proteomics would have been able to make and use the claimed positionally addressable arrays based

on knowledge available to those in the field in combination with the disclosure of the '781 application. It is also my opinion that any experimentation required for making and using the claimed positionally addressable arrays would have been routine and thus not inordinate or excessive. Therefore, it is my opinion that the rejection is in error, and I present herein the rationale upon which I base that conclusion.

6. As discussed in detail below, the specification of the '781 application clearly provides sufficient disclosure for a typical practitioner in the field of proteomics to make and use positionally addressable arrays comprising 61 purified, active yeast kinases. Based upon this disclosure, in combination with what was known at the time of filing of the present application, the use of kinases from other organisms, including mammals and *Drosophila*, in the preparation of the presently claimed positionally addressable arrays, would not have required undue experimentation, but rather, routine and straightforward experiments.

7. As set forth in the references discussed below, protein kinases and functional kinase domains used in the positionally addressable arrays that form the basis of the claims were, at the time this application was filed, all well-known, well-characterized proteins. For example as discussed in Hunter and Plowman, "The protein kinases of budding yeast: six score and more," *TIBS* 22:18-22 (1997) (hereinafter "Hunter and Plowman"):

[b]udding yeast has 113 convention protein kinase genes, corresponding to ~2% of the total genes (see Table 1 in cetrefold). More than 60% of these protein kinases have either known or suspected functions; the remainder are novel, and functional analysis awaits. In terms of defined functions encoded by the yeast

genome, protein kinases come in a close second behind transcription factors.

Hunter and Plowman at page 18, first column, first paragraph. A review by Manning *et al.*, "The Protein Kinase Complement of the Human Genome," *Science* 298:1912-1934 (2002) (hereinafter "Manning1"), indicates "[p]rotein kinases are among the largest families of genes in eukaryotes and have been intensively studied." Manning1 at page 1913, first column, first paragraph.

8. It is well recognized that kinases are highly conserved such that homologs exist between yeast and many other organisms. Furthermore, the regulation of the different kinases and the phosphorylation motifs of substrates recognized by related kinases are often the same, indicating that they behave similarly biochemically. As set forth in Manning *et al.*, "Evolution of protein kinase signaling from yeast to man," *TRENDS in Biochemical Sciences* 27:514-520 (2002) (hereinafter "Manning2"):

all major kinase groups and most kinase families are shared among metazoans, and many are also found in yeast, reflecting the breadth of conserved function mediated by kinases. This ancient conservation enables cross-species analysis of function, particularly of human kinases in simpler model systems. Of 209 subfamilies, 51 are present in all four genomes, and 144 are present in all metazoans, indicating that most divergence of kinases into specific functions and families occurred during early eukaryotic and metazoan evolution.

Manning2 at page 514, second column, first full paragraph, and at Figure 1 and Table 1. This known relationship is also addressed in Manning 1:

Phylogenetic comparison of the human kinome with that of yeast, worm, and fly confirms that most kinase families are shared among metazoans and defines classes that are expanded in each lineage. Of 189 subfamilies present in human, 51 are found in all four eukaryotic kinomes, and these

presumably serve functions essential for the existence of a eukaryotic cell. An additional 93 subfamilies are present in human, fly, and worm, implying that these evolved to fulfill distinct functions in early metazoan evolution. Comparison with the draft mouse genome indicates that more than 95% of human kinases have direct orthologs in mouse; additional orthologs may emerge as that genome sequence is completed.

Manning¹ at page 1914, last paragraph bridging first and second columns. *See also* Hunter and Plowman at page 20, second column, second paragraph, "[m]ost of the main vertebrate subfamilies of protein kinases are represented in yeast."

9. Furthermore, as function is often highly conserved, human kinases can be substituted for yeast kinases, illustrating the highly conservative nature of these proteins. *See Lee and Nurse, "Complementation used to clone a human homologue of the fission yeast cell cycle control gene cdc2," Nature 327: 31-35 (1987) (hereinafter "Lee and Nurse"):*

Because the human *CDC2Hs* gene can provide all of the functions of *cdc2Sp* in fission yeast it is reasonable to assume that it performs a similar role to *cdc2Sp* in controlling the human cell cycle. This conclusion is supported by the structural similarity between the two genes both in overall homology and size of the proteins. . . .

The identification of a *cdc2*-like function in human cells suggests that elements of the mechanisms by which the cell cycle is controlled will probably be found in all eukaryotic cells.

Lee and Nurse at page 35, first column to second column.

10. Therefore, at the time this application was filed, the "state of the art" in protein kinases was such that a practitioner possessing a typical level of skill in proteomics, such skill including but not limited to protein purification and analysis,

would have readily recognized from the '781 application, and the knowledge available in the art, that kinases of yeast, mammals and *Drosophila* could be utilized to practice the present invention.

11. The Examples set forth in the '781 application describe positionally addressable protein arrays made with purified, active kinases isolated from yeast. The specification describes that the purified, active yeast kinases were prepared by cloning yeast kinase genes into a high copy *URA3* expression vector. See the '781 application at page 26, lines 27-28. The plasmids containing the vector sequences were transformed into yeast, and Ura⁺ colonies were selected. Plasmids were rescued in *E. coli*, then transformed into the *pep4* yeast strain for kinase protein purification. Purified, active kinases were attached to polydimethylsiloxane (PDMS) chips, and the chips comprising the purified, active yeast kinases were assayed for the phosphorylation of 17 different substrates to determine *in vitro* kinase activity. This large-scale analysis of purified, active yeast kinases allowed me to characterize the activities of 119 protein kinases for 17 different substrates and to compare the functional relationship of these protein kinases to one another. This analysis also allowed me to determine meaningful biological interactions between these kinases and their targets.

12. As described above, the '781 application provides working examples where purified, active kinases from yeast were used to make a positionally addressable array. As described in the references cited above, those working in the field of proteomics at the time this application was filed were aware that yeast, mammalian and *Drosophila* kinases are highly conserved and homologous. See *e.g.*, Manning2. In

addition, the working examples in the specification provide a clear road map sufficient to allow a practitioner in the field of genomics and proteomics to extend the experiments with yeast kinases to mammalian and *Drosophila* kinases making such an extension routine. *See, e.g.,* the '781 application at pages 25-35. In particular, in my opinion, a typical practitioner in the field of proteomics would consider the production of an array using at least 61 purified, functional kinases from yeast as detailed in the specification sufficient to enable them to prepare arrays using purified, active kinases from other organisms, including mammals and *Drosophila*, especially in light of the specific reference to this use in the specification.

13. The Examiner has also rejected claims 1-11, 141, 181-186, 188 and 193-195 as allegedly being obvious in view of Uetz *et al.*, *Nature* 403:623-631 (February 10, 2000) (hereinafter "Uetz"). The Examiner contends that Uetz discloses a protein array comprising yeast genome encoded proteins, and that the proteins were expressed in 96-well plates. The Examiner asserts that the claimed kinases would have been inherent to the yeast array disclosed in Uetz, since yeast inherently contain kinase in their structure, or that they would have been obvious to determine given the identified genome of yeast. It is my opinion that there is no disclosure in Uetz, inherent or otherwise, of an array or the construction of an array of at least 61 kinases or functional kinase domains, in which the array comprises kinases that are *purified and active*, as required by present claim 1. At the time of filing of the present application, as set forth below, it was unexpected that kinases and functional kinase domains of these kinases, could be purified and placed on a solid support to form an array, and that these kinases and kinase domains, *would retain their kinase activity*. Skeptics in the field, before, and even well after the time the

present application was filed, thought that the proteins used to make the array of the presently claimed invention would denature and, therefore, be inactive. It was an unexpected and surprising result that the purified proteins on the array retained their activity and could be utilized to determine meaningful biological interactions between the purified, active kinases and their targets (such as enzyme-enzyme or enzyme-substrate interactions). Simply put, it is only after the guidance provided in the present specification that a practitioner in the field of proteomics would consider it possible to generate the presently claimed arrays.

14. The following exemplary references describe the skepticism from those in the field regarding the preparation of protein arrays both before and after the time of filing of the present application, as well as some of the problems regarding preparation of protein arrays comprising large numbers of purified active proteins that were overcome by the presently claimed invention.

15. Anderson, K.S. and LaBaer, J., *Journal of Proteome Research* 4:1123-1133 (March 30, 2005) (hereinafter "Anderson and LaBaer") state that

[t]heir theoretical advantages notwithstanding, protein microarrays have still not found widespread use, in part because producing them is challenging. Historically, it has required the high-throughput production and purification of protein, which then must be spotted on the arrays. Once printed, concerns remain about the shelf life of proteins on the arrays.

Anderson and LaBaer, page 1129.

16. Shaw, G., *Drug Discovery and Development* (February 3, 2005) (hereinafter "Shaw") states that:

[i]t was first thought that protein biochips would just be an extension of DNA microarrays, and that hasn't exactly panned out," says Bodovitz. That's because proteins have proven to be much trickier to work with in array format than their genomic counterparts. First of all, there are issues of stability. Membrane proteins, for example, make up the majority of potential drug targets, but they're particularly challenging to stabilize. Then there's the choice of immobilization technique, which determines how well the target protein presents itself to the capture agent, and the problem of nonspecific binding. And of course, proteins are inherently unstable outside their natural habitat of living cells, making them much more challenging than DNA to tag and manipulate.

Shaw at page 1.

17. As set forth in the following references, it was well known that spotting proteins on solid surfaces often resulted in protein denaturation caused by uncontrolled absorption, thereby inactivating the proteins. *See* Abstract of both Tleugabulva *et al.*, "Evidence for the denaturation of recombinant hepatitis B surface antigen on aluminum hydroxide gel," *J. Chromatogr. B. Biomed. Sci.* 702:153-163 (1998); and Servagent-Noinville *et al.*, "Conformational Changes of Bovine Serum Albumin Induced by Absorption on Different Clay Surfaces: FTIR Analysis," *J. Colloid Interface Sci.* 221:273-283 (2000).

18. Prior to the presently claimed invention, only small numbers of proteins, and/or inactive proteins, were able to be displayed on an array. It is only after the teaching of the '781 application that large numbers of purified proteins were able to be placed on a solid support, in the recited density, such that they remained active. In Bussow *et al.*, "A method for global protein expression and antibody screening on high-density filters of an arrayed cDNA library," *Nucleic Acids Res.* 26: 5007-5008 (1998) (hereinafter "Bussow1"), large scale protein arrays were produced, but only using

denatured proteins. ("These protein filters were processed on pre-soaked blotting paper, i.e., denatured in 0.5 M NaOH, 1.5 M NaCl for 10 min, neutralized for 2x5 min in 1 M Tris-HCl, pH 7.5, 1.5M NaCl and incubated for 15 min in 2x SSC. Filters were air-dried and stored at room temperature." Bussow1 at page 507, second column, first paragraph.) Similarly, in Bussow *et al.*, "A human cDNA library for high-throughput protein expression screening," *Genomics* 65:1-8 (2000) (hereinafter "Bussow2"), denaturing conditions were used to prepare the protein arrays. ("Twenty-five microliters of 50% N-NTA agarase was added to protein extracts obtained under denaturing conditions." Bussow2 at page 2, first column, third paragraph.) In addition, in the introduction of Bussow2, the authors discuss the difficulties in producing large amounts of purified proteins and maintaining their activity when placed on an array:

the individuality of protein molecules demands highly customized procedures for their expression. Automation of these procedures requires systems that allow the efficient handling of large numbers of clones representing many different proteins. Bacterial systems are easy to manage *but the expression of eukaryotic proteins can be problematic*, due to aggregation, formation of insoluble inclusion bodies, and/or degradation of the expression product. Eukaryotic systems suffer from lower yields of heterologous protein (e.g. *Saccharomyces cerevisiae*s), high demands on sterility (e.g. mammalian systems) or time consuming cloning procedures (e.g. Baculovirus system).

Bussow at page 1, last paragraph bridging first and second columns (citations emitted, emphasis added). Thus, rather than attempt to overcome these various issues, the authors proceeded to produce denatured proteins in *E. coli* for use in their arrays. Similarly, Lueking *et al.*, "Protein microarrays for gene expression and antibody screening," *Anal. Biochem.* 270:103-111 (1999) (hereinafter "Lueking"), also prepared protein arrays

utilizing denaturing conditions (6M guanidinium-HCl, 0.1M NaH₂PO₄, 0.01 M Tris-HCl, pH 8.0, Lueking at page 104, second column, first paragraph).

19. In Ge, "UPA, a universal protein array system for quantitative detection of protein-protein, protein-DNA, protein-RNA and protein-ligand interactions," *Nucleic Acids Research* 28:e3(i-vii), the author was only able to produce arrays comprising 48 proteins at a very low density, utilizing a traditional purification format. Extension of this disclosure to arrays comprising at least 100 different substances per cm² would have required extensive, additional experimentation beyond the scope of the disclosure provided in this reference.

20. Thus, as noted in the references cited above, it is my opinion that experts in the field were clearly skeptical of the ability to prepare protein arrays comprising large numbers of purified, active enzymes, at the densities recited in the presently claimed invention. Instead, denaturing conditions or traditional purification methods on small numbers of proteins were required. Absent the teachings of the '781 application there was no reasonable expectation that arrays comprising at least 100 different substances per cm², wherein the substances comprise 61 purified, active kinases on a solid support, could be successfully prepared, at the time of filing of the present application.

21. It is only after the guidance of the present specification, specifically the methods described in the present application which allowed for large-scale purification and arraying of active kinases or functional kinase domains, that preparation of the presently claimed positionally addressable arrays was possible. The methods of the present invention, as discussed below, are suitable for rapidly purifying large numbers of

samples, such as the purification of active kinases isolated from mammalian, yeast, and *Drosophila*. As an example, yeast kinases were purified by growing different strains of *pep4* yeast cells, each containing a plasmid encoding a single GST-tagged kinase gene, in 96-well plates. Galactose was added to induce protein expression. The cultures of the same strain were combined, washed, resuspended and lysed. The GST fusion proteins were purified from these strains using glutathione beads and standard protocols in a 96-well format. This method allowed for the purification of a high number of yeast kinases in a relatively short amount of time. The buffers and methods used also ensured that the purified kinases or functional kinase domains retained their activity. *See* Example 1 of the '781 application at page 26, line 25, through page 27, line 19.

22. Positionally addressable arrays were then prepared using the purified, active proteins purified as described above. Arrays were made from polydimethylsiloxane (PDMS) (Dow Chemical, USA), which was cast over microfabricated molds. Liquid PDMS was poured over the molds and, after curing flexible silicone elastomer array sheets were then peeled from the reusable molds. Arrays were immersed in 3-glycidooxypropyltrimethoxysilane linker (GPTS) in order to facilitate adsorption of protein to the wells. To attach proteins to the chips, protein solutions were added to the wells and incubated on ice for 1 to 2 hours. After rinsing with cold HEPES buffer, the wells were blocked with BSA in PBS. *See* Example 1 of the '781 application as filed at page 27, line 21, through page 28, line 9.

23. The methods set forth in the present application are sufficient to enable a typical practitioner in the field of proteomics to make and use positionally addressable

arrays comprising 61 purified, active kinases of yeast, mammals and *Drosophila*. Furthermore, such methods were only available upon filing of the present application.

24. The Examiner has also rejected claims 1-11, 141, 164, 169, 173, 174, 177, 181-186, 188 and 193-195 as allegedly being unpatentable over Shalon (WO 95/35505; hereinafter "Shalon") in view Felder *et al.* (U.S. Patent No. 6,458,533; hereinafter "Felder") of Lafferty (U.S. Patent No. 6,972,183; hereinafter "Lafferty").

25. The Examiner contends that Shalon discloses a microarray having regions with a density of at least about 100/cm², and that the arrays can comprise enzymes. The Examiner notes, however, that Shalon does not disclose arrays comprising kinases. The Examiner relies on the disclosures of Felder or Lafferty to cure this deficiency. Specifically, the Examiner contends that Felder discloses that kinases are enzymes, and the Lafferty discloses an array containing substrate-enzymes, such as kinases. The Examiner therefore concludes that it would have been obvious to prepare the array disclosed in Shalon using the kinases disclosed in Felder and Lafferty, and hence, the presently claimed invention is rendered obvious.

26. Shalon is primarily directed to arrays comprising polynucleotides (*see* Examples 1-3), and only mentions in passing that arrays comprising proteins and enzymes could be constructed. Furthermore, Felder discloses preparation of arrays comprising peptides that are *substrates* for kinases, not arrays comprising the kinases themselves, "[a] chimeric linker molecule is prepared in which a 25 base pair oligonucleotide complementary to one of the anchors is crosslinked to a *peptide substrate of a tyrosine phosphokinase enzyme*." Felder at column 44, lines 18-21

(emphasis added). Thus, Felder does not disclose the preparation of arrays comprising 61 purified active kinases or functional kinase domains thereof, as required by present claim 1.

27. With regard to Lafferty, it is important to note that the arrays disclosed therein are limited to enzymes expressed in expression library cells, and that Lafferty does not disclose the purification of these enzymes prior to placement on a solid support, as recited in the presently claimed invention. Lafferty states, at column 18, lines 1-14:

The library comprises a plurality of recombinant clones, which comprise host cells transformed with constructs comprising expression vectors into which have been incorporated nucleic acid sequences derived from the DNA samples. One or more substrates and at least a subset of the clones is then introduced, either individually or together as a mixture, into capillaries (all or a portion thereof) in a capillary array. Interaction (including reaction) of the substrate and a clone expressing an enzyme having the desired enzyme activity produces an optically detectable signal, which can be spatially detected to identify one or more capillaries containing at least one signal-producing clone. The signal-producing clones can then be recovered from the identified capillaries.

Therefore, Lafferty does not disclose arrays comprising 61 purified active kinases, as set forth in the presently claimed invention.

28. Therefore, it is my opinion that Shalon, Felder and Lafferty, alone or in combination, do not disclose the presently claimed positionally addressable arrays, specifically, arrays comprising 61 purified active kinases or functional kinase domains thereof, as set forth in present claim 1. Specifically, the references cited by the Examiner do not disclose preparation of purified kinases which are then placed on a solid support, as recited in present claim 1. Thus, there are clearly differences between the cited

references and the presently claimed invention that have not been addressed by the Examiner.

29. As set forth in detail above, there was no reasonable expectation of success of preparing an array comprising at least 61 purified active kinases or functional kinase domains of these kinases, based on the references cited by the Examiner. At the time of filing of the present application, experts in the field were skeptical, and it was unexpected, that purified kinases and functional kinase domains of these kinases, could be placed on a solid support to form an array, and that these proteins would retain their activity. It was also unexpected that these positionally addressable arrays could be used to determine meaningful biological interactions (such as enzyme-enzyme or enzyme-target interactions) between the purified active kinases and their targets. It is only after the guidance of the present specification that a typical practitioner in the field of proteomics would be able to generate the presently claimed arrays.

30. As discussed above, it is my opinion that, at the time of filing of the present application, it was unexpected that purified kinases and functional kinase domains of these kinases could be purified and placed on a solid support to form an array. It is also my opinion that it was unexpected that the purified kinases and functional kinase domains of these kinases would retain their activity when placed onto the array. It is only after the guidance provided in the present specification that a person of ordinary skill in the art would consider it possible to generate the presently claimed arrays.

31. I conclude that for at least the reasons stated above that there was no reasonable expectation of success of preparing an array comprising at least 61 purified active kinases or functional kinase domains of these kinases. It is my opinion that, at the time of filing of the present application, experts in the field were skeptical, and it was unexpected, that purified kinases and functional kinase domains of these kinases could be placed on a solid support to form an array, and that these proteins would retain their activity. It is only after the guidance of the present specification that a typical practitioner in the field of proteomics would be able to generate the presently claimed arrays.

32. I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the present patent application or any patent issued thereon.

Respectfully submitted,

Date: 4/13/09

A handwritten signature in dark ink, appearing to read 'Michael Snyder', is written over a horizontal line.

Michael Snyder

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Education

1973-1977 B.A. University of Rochester, Rochester, New York
 Chemistry and Biology
 1978-1982 Ph.D. California Institute of Technology, Pasadena, California
 Department of Biology, Degree conferred 6/83

Professional Experience

1977-1978 Research Assistant, Department of Biology, University of
 Rochester, Rochester, New York
 1978-1982 Graduate Student with Dr. Norman Davidson, California Institute
 of Technology, Pasadena, California
 1982-1986 Postdoctoral Fellow with Dr. Ronald W. Davis, Department of
 Biochemistry, Stanford University School of Medicine,
 Stanford, California
 1986-1990 Assistant Professor, Department of Biology, Yale University,
 Connecticut
 1990-1997 Associate Professor, Department of Biology, Yale University,
 Connecticut (tenured 1994)
 1997-present Professor, Dept. of Biology (now Mol. Cell. Devel. Biol.), Yale Univ., CT
 1991-present Member Yale Comprehensive Cancer Center
 1992-present Associate Professor/Professor (Joint Appointment), Department of
 Molecular Biophysics and Biochemistry, Yale University
 1998-2004 Chair, Dept. of Molecular, Cellular and Developmental Biology, Yale Univ.
 (Dept. doubled in size and 3X in funds during my tenure).
 2002-present Director, Yale Center for Genomics and Proteomics
 2006-present Genetics Society of America Council Member (Elected)
 2006- 2008 President, US HUPO (Elected)

Academic Honors/Fellowships

1978-1982 NIH Predoctoral Training Fellowship
 1982-1985 Helen Hay Whitney Postdoctoral Fellowship
 1986 United Scleroderma Foundation Award
 1987-1991 Pew Scholar Award
 1989 Yale Junior Faculty Fellowship
 2000-2005 Burroughs Wellcome Scholar Award
 2002 Genome Technology Finalist in Microarray Masters
 2002-present Appointed Lewis B. Cullman Professor of MCDB
 2007 Connecticut Medal of Science

Advisory Committees

1989,90, 94-98, Member NIH Study Section- Ad hoc Reviewer

2000-07	
1993	Scientific Advisory Board Review Panel-American Cancer Society
1994-96	Howard Hughes Predoctoral Fellowship Review Committee
2002	Damon Runyan Walter Winchell Review Panel
1996-2002	March of Dimes Grant Review Panel
1997	ATCC Advisory Committee
1999	NSF Division Review Panel
2000, 2002	NIH Study Section Review Working Group
2000	Canadian Genome Center Review Panel
2001-present	Northeast Structural Genomics Consortium Scientific Advisory Committee
2001-present	Member, Institute of Genetics Advisory Council, CIHR Canada
2002-2007	Member, Ontario Genome Institute Scientific Advisory Board
2002-present	Member, Chinese National Human Genome Institute Advisory Board
2007-present	SAB, Integrated Genomics Project Univ. of Toronto
2008-present	SAB, Duke Univ. Systems Biology Center
2003-2006	SAB, Blueprint Initiative
2003	NIH Special Road Map Advisory Committee
2003	External Reviewer, Dept. of Medical Genetics, Univ. of Toronto
2003-present	Scientific Advisory Board, Gottenberg Univ. Genomics Meeting
2004-2007	Damon Runyan-Walter Winchell Review Panel
2007	NSF Plant Genomics Initiatives 5 Year Review
2008	External Review Committee, Gene Expression Unit, EMBL

Meeting Organizer

1994	Coorganizer, Juan March Meeting on Signal Transduction & Morphogenesis
1996	Chair, FASEB Meeting: Yeast Chromosome Structure, Repl. & Segregation
2000	Yeast Genetics Meeting Program Committee
2004	CoOrganizer, ASBMB Genomics, Proteomics and Bioinformatics Meeting*
2004	CoOrganizer, GSA International Meeting on Yeast Molecular Genetics
2004	CoOrganizer, CSH Plant Genomes: From Sequence to Phenomes
2006	CoOrganizer, ASBMB Genomics, Proteomics and Bioinformatics Meeting
2006	Organizer, GSA International Meeting on Yeast Molecular Genetics*
2006	CoOrganizer, US HUPO
2007	CoOrganizer, CSH Plant Genomes: From Sequence to Phenomes
2007	CoOrganizer, Keystone Meeting on Functional Genomics

Editorial Boards

1996-2000	Editorial Board, The Dynamic Cell
2001-2004	Editorial Board, Chemistry and Biology
2000-2006	Editorial Board, FEMS Yeast Research
2000-present	Editor-in-Chief (until 2002; now Editor) Functional and Integrative Genomics
2001-present	Editorial Board, Molecular and Cellular Proteomics
2002-present	Editorial Board, Drug Discovery Today
2004- present	Editorial Board, PloS Genetics
2005-present	Editorial Board, Genes and Development
2005-present	Editorial Board, Molecular Systems Biology

Named/Distinguished Lectureships (starting 2004)

2004	California Institute of Technology, Norman Davidson Lecture
2004	University of Chicago, Fredrick Setiz Lecture

- 2004 Tulane University, Gerber Lecture
- 2004 University of Iowa, Raymond Fung Lecture
- 2006 Northeastern University, Hoehn Lecture
- 2007 EBI Distinguished Lecturer
- 2008 Northwestern University Distinguished Lectureship
- 2008 Fred Sherman Lecture, Univ. of Rochester

Keynote/Featured Speaker

- 2000 University of Sherbrooke Graduate Symposium*
- 2001 CHI: Functional Genomics
- 2002 Yale University Pathology Retreat
- 2002 Georgia Bioinformatics Symposium
- 2003 University of Texas Medical Faculty Symposium
- 2003 Structural and Functional Genomics, Singapore
- 2004 International Meeting On Arabidopsis*
- 2004 Pennsylvania State Graduate Student Symposium
- 2005 Keystone Conference on Plant Signaling
- 2005 New York University: Genomics Symposium—Genomes in Action
- 2005 Chip to Hits
- 2005 Systems Biology Meeting
- 2006 AGCT Genomics Meeting
- 2006 Genomes to Biology Meeting, Manchester, UK
- 2006 Keystone Conference on Plant Abiotic Stress
- 2006 CHI Genes to Targets
- 2006 AUHUPO*
- 2007 ABRF*
- 2007 Pan American and Brazilian Biochemistry and Molecular Biology Meeting*
- 2007 Uppsala Neuroscience Center Launch
- 2007 IBC Diagnostics 2 Discovery
- 2007 DREAM 2 Conference
- 2008 CHI Mining the Plasma Proteome
- 2008 Student Invited Speaker, Vanderbilt Genetics Retreat
- 2008 Genetics Day, Univ. of Rochester

*Meetings attended by over 900 people

Commercial Activity

Topogenetics/Exelexis 1990-1991 Partial Founder
 Genaissance 1999-2001 Scientific Advisory Board (SAB)
 Mycota 1996-2000 SAB
 Protometrix 2001-2004 (now subsidiary of Invitrogen) Founder and Chair of SAB
 RxGen 2003-present SAB
 Affomix 2006- Present Founder and Chair of SAB

Publications

1. Kung LA*, Tao S-C*, Qian J, **Snyder M**, Zhu H. Global analysis of the glycoproteome in *S. cerevisiae* reveals new roles for protein glycosylation in eukaryotes. Submitted.
2. Korbel JO, Kim PM, Chen X, Urban AE, Weissman S, **Snyder M**, Gerstein MB. The current excitement about copy-number variation: how it relates to gene duplications and protein families. *Curr Opin Struct Biol*. 2008. [Epub ahead of print] PMID: 18511261

3. Lian Z, Karpikov A, Lian J, Mahajan MC, Hartman S, Gerstein M, **Snyder M**, Weissman SM. A Genomics Analysis of RNA polymerase II modification and chromatin architecture related to 3' end RNA polyadenylation. *Genome Res.* 2008 May 16. [Epub ahead of print] PMID: 18487515.
4. Nagalakshmi U, Wang Z, Waern K, Shou C, Raha D, Gerstein M, **Snyder M**. The Transcriptional Landscape of the Yeast Genome Defined by RNA Sequencing. *Science.* 2008 May 1. [Epub ahead of print] PMID: 18451266
5. Wu JQ, **Snyder M**. RNA polymerase II stalling: loading at the start prepares genes for a sprint. *Genome Biol.* 2008 May 2;9:220. PMID: 18466645
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